HHS Public Access

Author manuscript

J Am Coll Radiol. Author manuscript; available in PMC 2020 August 20.

Published in final edited form as:

J Am Coll Radiol. 2018 March ; 15(3 Pt B): 543–549. doi:10.1016/j.jacr.2017.12.006.

Translational Radiomics: Defining the Strategy Pipeline and Considerations for Application—Part 2: From Clinical Implementation to Enterprise

Faiq Shaikh, MD[a], **Benjamin Franc, MD, MS, MBA**[b], **Erastus Allen, MBA**[c], **Evis Sala, MD, PhD**[d], **Omer Awan, MD, MPH**[e], **Kenneth Hendrata, MBA**[f], **Safwan Halabi, MD**[g], **Sohaib Mohiuddin, MD**[h], **Sana Malik, DrPH**[i], **Dexter Hadley, MD, PhD**[j], **Rasu Shrestha, MD, MBA**[k]

[a]Institute of Computational Health Sciences, UCSF, San Francisco, California.

[b]Department of Radiology and Biomedical Imaging, UCSF, San Francisco, California.

[c]UPMC Enterprises, Pittsburgh, Pennsylvania.

[d]Department of Radiology, Memorial Sloan Kettering Cancer Center, New York, New York.

[e]Department of Radiology, Temple University, Philadelphia, Pennsylvania.

[f]Carnegie Mellon University, Pittsburgh, Pennsylvania.

[g]Department of Radiology, Stanford University, Palo Alto, California.

[h]Department of Radiology, Division of Nuclear Medicine, University of Miami, Miami, Florida.

[i]School of Social Welfare, Stony Brook University, New York, New York.

[j]Institute of Computational Health Sciences, UCSF, San Francisco, California.

[k]UPMC Enterprises, Pittsburgh, Pennsylvania.

Abstract

Enterprise imaging has channeled various technological innovations to the field of clinical radiology, ranging from advanced imaging equipment and postacquisition iterative reconstruction tools to image analysis and computer-aided detection tools. More recently, the advancement in the field of quantitative image analysis coupled with machine learning-based data analytics, classification, and integration has ushered in the era of radiomics, a paradigm shift that holds tremendous potential in clinical decision support as well as drug discovery. However, there are important issues to consider to incorporate radiomics into a clinically applicable system and a commercially viable solution. In this two-part series, we offer insights into the development of the translational pipeline for radiomics from methodology to clinical implementation (Part 1) and from that point to enterprise development (Part 2). In Part 2 of this two-part series, we study the components of the strategy pipeline, from clinical implementation to building enterprise solutions.

Corresponding author and reprints: Faiq Shaikh, MD, Institute of Computational Health Sciences, University of California San Francisco, San Francisco, CA, USA; faiq.shaikh@hotmail.com.

The authors have no conflicts of interest related to the material discussed in this article.

Keywords

Radiomics; enterprise; translational; precision; medicine; radiology

INTRODUCTION

Radiomics can be defined as the process of uncovering signals buried within images and using such signals to augment the traditional radiologic interpretation and gain insights into the structure, behavior, and therapeutic response profile of a disease. We define translational radiomics as a process of converting the basic radiomic methodologies into evidence-based clinically applicable models that may then undergo the steps of platform standardization, algorithm integration, and applied business intelligence to create a commercialized product for mainstream use.

In this part (Part 2), we identify the steps involved in the process of translating a clinically viable radiomics tool to a successful enterprise solution to include the following components: understanding the most applicable areas for clinical implementation of radiomics, performing outcomes analysis to which radiomic features may be associated, implementing radiomics in a platform that can help guide physician behavior, and identifying ways to continually improve the radiomics algorithms as exponentially increasing data and features are generated in the path toward precision medicine (see Fig. 1).

APPLICATIONS FOR CLINICAL RADIOMICS

Image Interpretation and Direct Image Analysis

Perhaps the most direct application of radiomics from an imaging physician's standpoint is to improve or facilitate the interpretation of images, as has been investigated in evaluating levels of fibrosis on ultrasound imaging of the liver [1], classifying neurodegenerative disease on MRI [2], and classifying bone tumors on PET-CT [3]. In a sense, this type of application represents an extension of computer-assisted detection and classification and has seen prior direct application in the realms of lung nodule classification or breast cancer detection.

Incorporation of radiomics into other aspects of image analysis stretches the field's utility into the realm of image-guided therapy. The use of feature analysis for more precise delineation of anatomic boundaries in cardiology or vascular images has the potential to improve the segmentation process for quantitative volumetric analyses themselves or to delineate boundaries or track them for treatment purposes [4–6]. Feature-based tumor boundary delineation has applications in staging as well as radiation oncology treatment planning [7–9].

Precision Medicine—Imaging Phenotypes to Guide Therapy

The realization that diseases and their relationships cannot be understood or treated effectively using traditional disease classifiers has led to the concept of precision medicine. Precision medicine seeks to accurately identify the true nature of disease to apply highly

targeted therapeutic agents to achieve an optimal response [10]. The opportunity to bring imaging directly into precision medicine, as both genomics and proteomics and other "omics"-related fields, is one of the most intriguing areas of radiomics' growth. One of the most aggressively pursued applications of radiomics has been in identifying imaging phenotypes in cancer [11–13]. These phenotypes may or may not have corresponding detectable proteomic or genomic correlates and may be used independently to predict survival, select patients for specific therapies, assess response to systemic or targeted therapies, or otherwise guide therapy [14–22]. By identifying noninvasive means to characterize the whole tumor, rather than based on results of a single needle core biopsy, assessment of the patient's future risk may be more accurately identified, allowing selection of a more appropriate course of neoadjuvant or adjuvant therapy as well as improved assessment of response to therapy [23–31].

Textural feature analysis has likewise been employed to understand microstructure in nononcologic applications such as cardiovascular disease [32,33]. Feature changes in atherosclerotic plaques [34–37] and abdominal aortic aneurysms [38] have implications for important disease evolution [39–41].

CONNECTING RADIOMICS TO OUTCOMES—HIGHLIGHTS OF THE PROCESS

Radiomics in Clinical Trials

There is a need to incorporate radiomics and radiogenomics into existing and future clinical trials, to codevelop radiomics feature-based criteria for treatment response. For example, because existing treatment response criteria, such as response evaluation criteria in solid tumors, immune-related response criteria, World Health Organization classification, and PET response criteria in solid tumors, do not address the problem of pseudoprogression, integrating radiomics-based response assessment into new immuno-therapy trials should be a priority (Fig. 2).

Incorporation of robust radiomics biomarkers into the design of new clinical trials will increase the rate of convergence onto those feature sets that provide the most information about treatment response. Radiomics can be paired with genomics and circulating tumor deoxyribonucleic acid (liquid biopsy) to develop multidimensional diagnostic-prognostic assessment solutions. A concerted effort between entities such as the Eastern Cooperative Oncology Group and ACR Imaging Network, and between the Quantitative Imaging Biomarkers Alliance and RSNA, is under way to meet these challenges.

Extracting Features to Assess as Predictors of Clinical Outcomes.—The first step toward achieving radiomics analysis of specific volumes that include tumor, other specified lesions, vasculature, or organs is to segment the volume of interest using one of a number of approaches, most of which entail manual, or at best, semi-automated segmentation strategies [42]. A number of such methods have been described by other authors, including region growing methods, level set methods, graph cut methods, active

contours (snake) algorithms, and semi-automatic segmentations such as live wires, among others [43–45].

Defining Clinical Outcomes to Which Radiomics Features May Be Compared.—Clinical outcome is often not a single predefined number. Seemingly straightforward concepts, such as overall survival or progression-free survival, are at times difficult to extract from electronic medical records or other informatics sources. Other outcome variables might include more complex concepts such as significant cardiac events, the performance of one or more specified procedures, clinical biomarkers, and so on.

Transforming clinical medical records into outcomes requires extraction of both structured and unstructured data from the electronic health record. Structured information provides specific events or therapies to be placed on clinical timelines relative to the imaging event on which radiomics is being performed. To address the need for standardization of clinical context in the electronic health record in a manner that can be processed in a meaningful way using information technology tools, many clinical and biomedical ontologies have been developed over decades, such as the Systematized Nomenclature of Medicine–Clinical Terms developed by the International Health Terminology Standards Development Organization, which standardizes clinical terminology and physician phrases in multiple languages and is widely used in the exchange of electronic health information [46–50].

The unstructured information in free-text fields (eg, physician's notes) requires a sophisticated review of clinical notes and other free-text entries to piece together the patient's medical condition and the timeline of events to achieve quantifiable outcomes, such as progression-free survival in the case of oncology. Basic strategies, such as word tokenization and part-of-speech tagging, can be initially employed; however, higher forms of natural language processing and artificial intelligence (AI)–based methodologies are often required to contextualize events in the medical record [51–58]. Open source natural language processing tools have been developed specifically for application in medical contexts, such as the clinical Text Analysis Knowledge Extraction System and Python Natural Language Toolkit [59–61].

Analyzing Relationships Between Radiomic Feature Sets and Clinical Outcomes.—After understanding the collection of clinical measures that must be made or the genomic or proteomic parameters to which radiomic data are to be correlated, an analysis plan must be constructed. Tests of the stability and reproducibility of features must be incorporated into the study [62]. Radiomics features can number in the thousands, and generally the outcome variables will be drawn from patients numbering an order of magnitude fewer; therefore, care must be taken to avoid the identification of statistically significant findings due to random chance [63]. A number of means of dealing with this issue in the context of this type of discovery research exist [64–68].

Implementing Radiomics in a Platform That Impacts Physician Practice.—Full integration of radiomics in clinical radiology requires a close collaboration between radiologists and computer scientists. Radiologist engagement goes beyond building a pleasing user interface; radiologists will be asked to embrace a shift from a chiefly

qualitative use of imaging to a form of imaging assessment in which quantitative assessment is integral. In addition, radiologists will be asked to heavily rely on results obtained through AI methods. Identifying liaisons in the radiology community to educate peers and serve as resources for those wary of AI will both facilitate the translation of radiomics into clinical practice and ensure that the radiology specialty maintains its central role as medicine's information science specialty.

New technologies, especially if they involve using results from an automated or a semi-automated computational system, can take time before they are universally accepted across medicine. Once results of a radiomics-driven clinical decision support system are clinically validated through outcomes research, it will provide a more robust evidence base to implement radiomics in the practice of precision medicine. Furthermore, in the era of value-based care, evidence of value improvement and cost reduction based on radiomics would further facilitate radiomic's move into mainstream standard of care.

Crowdsourcing Algorithms

Any data-driven technology requires methodologies to improve based on new information. The roles of deep learning and AI, in general, are integral to radiomics because they enable this type of continuous improvement based on incredibly large sets of new data generated in the clinic each day. The crowdsourcing of algorithms, such as through the popular Kaggle competition website, is a method to obtain insights from a large population of data scientists. Competition participants are often rewarded with recognition and, for top performers, monetary consideration [69], although solutions in the radiomics space will also require a balance between high predictive performance and solution distinctiveness. A large challenge of this crowdsourcing approach is navigating regulatory and institutional requirements in sharing data broadly. Although adding complexity and constraining knowledge discovery, homomorphic encryption may offer a mechanism to address these concerns [70].

Product Development and Product Management

As solutions are developed, they should be tested with feedback from users to allow greater future enhancement, tailored to each health care enterprise system for most optimum use. Closed loop feedback between radiologists and referring physicians will ensure success and future updates to the software tools. Institutions often find it challenging to get buy-in from its users—the medical professionals who deliver health care—because new technology can often mean increased workload, distraction, or risk, even at the promise of better, faster, or cheaper patient care in the future. The design of the software should make it as a seamless part of the work-flow, using principles of user- or human-centered design and iterative software development.

When evaluating the feasibility of radiomics for day-to-day patient care, an institution must consider a strategy to develop and scale a solution, an approach surrounding the adoption of such solution, and the manpower it will take to deploy that solution. Because the field of radiomics is still emerging, a ready solution to put the science into practice may not exist and an institution may likely need to customize proxy solutions, piece together components, or even build some components from the ground up. For any of these cases, the institution

will need dedicated product management personnel and an experienced software architect. Scalability considerations will include server and database selection, data and network architecture, as well as the development platform.

Several academic centers and commercial entities have developed radiomics platforms, and ensuring that these platforms produce comparable radiomics feature measurements and that any studies underlying predictive analytics applications follow a set of prescribed guidelines should help to facilitate a coordinated effort to move translational radiomics into the precision medicine mainstream [71–74].

Marketing Radiomics With Comparative Performance Analysis

Driving the adoption of radiomics to the enterprise requires effectively communicating the value proposition to both internal stakeholders and commercial entities. Internal stakeholders, including leaders among clinical practitioners, will benefit from an examination of not only a comparison of the aggregate performance of professional image interpreters versus algorithms, but from a comprehensive analysis of the value of the data added by radiomics and how the performance and value differs according to subject characteristics and the targets of interpretation. CDS tools will need to be available to assist in the organization and interpretation of the volumes of data that radiomics analyses may generate [75].

Mainstream application of any technological advancement in medicine is subject to an evidence-based impact on clinical outcomes and, increasingly, on performance on the value-to-cost model [76]. Radiomics and imaging genomics hold great promise on that front—guiding precision biopsy, predicting and evaluating response to neoadjuvant chemotherapy, predicting response to immunotherapy, and deciphering pseudoprogression. If a radiomics solution is shown to decrease hospital stays or visits, to reduce the number of avoidable imaging studies and interventions, to allow for targeted therapy that avoids trying conventional lines of medication, and, in doing so, to favorably impact the health care financial bottom line, then it will be embraced as an effective as well as efficient state-of-the-art component of health care delivery.

CONCLUSION

There are several key steps in the translation of radiomics techniques to commercially implementable enterprise solutions. Further translation of radiomics to enterprise is still a novel concept, and we have introduced a framework that identifies its unique challenges and attempt to provide a pathway to mainstream application that improves outcomes.

REFERENCES

1. Gao S, Peng Y, Guo H, Liu W, Gao T, Xu Y, Tang X. Texture analysis and classification of ultrasound liver images. Biomed Mater Eng 2014;24:1209–16. [PubMed: 24212015]
2. Zhang J, et al. Texture analysis of multiple sclerosis: a comparative study. Magn Reson Imaging 2008;26:1160–6. [PubMed: 18513908]
3. Xu R, et al. Texture analysis on (18)F-FDG PET/CT images to differentiate malignant and benign bone and soft-tissue lesions. Ann Nucl Med 2014;28:926–35. [PubMed: 25107363]

4. Bogowicz M, et al. Stability of radiomic features in CT perfusion maps. Phys Med Biol 2016;61:8736–49. [PubMed: 27893446]
5. Echegaray S, et al. A rapid segmentation-insensitive “digital biopsy” method for radiomic feature extraction: method and pilot study using CT images of non-small cell lung cancer. Tomography 2016;2: 283–94. [PubMed: 28612050]
6. Kolossvary M, et al. Cardiac computed tomography radiomics: a comprehensive review on radiomic techniques. J Thorac Imaging 2018;33:26–34. [PubMed: 28346329]
7. Bagci U, et al. Predicting future morphological changes of lesions from radiotracer uptake in 18F-FDG-PET images. PLoS One 2013;8: e57105. [PubMed: 23431398]
8. Mu W, et al. Staging of cervical cancer based on tumor heterogeneity characterized by texture features on (18)F-FDG PET images. Phys Med Biol 2015;60:5123–39. [PubMed: 26083460]
9. Shiradkar R, et al. Radiomics based targeted radiotherapy planning (Rad-TRaP): a computational framework for prostate cancer treatment planning with MRI. Radiat Oncol 2016;11:148. [PubMed: 27829431]
10. National Research Council, D.o.E.a.L.S. Committee on a framework for developing a new taxonomy of disease, toward precision medicine: building a knowledge network for biomedical research and a new taxonomy of disease. Washington, DC: National Academies Press; 2011.
11. Aerts HJ, et al. Decoding tumour phenotype by noninvasive imaging using a quantitative radiomics approach. Nat Commun 2014;5: 4006. [PubMed: 24892406]
12. Ha S, et al. Autoclustering of non-small cell lung carcinoma subtypes on (18)F-FDG PET using texture analysis: a preliminary result. Nucl Med Mol Imaging 2014;48:278–86. [PubMed: 26396632]
13. Lambin P, et al. Radiomics: extracting more information from medical images using advanced feature analysis. Eur J Cancer 2012;48:441–6. [PubMed: 22257792]
14. Cheng NM, et al. Zone-size nonuniformity of 18F-FDG PET regional textural features predicts survival in patients with oropharyngeal cancer. Eur J Nucl Med Mol Imaging 2015;42:419–28. [PubMed: 25339524]
15. Cheng NM, Fang YH, Yen TC. The promise and limits of PET texture analysis. Ann Nucl Med 2013;27:867–9. [PubMed: 23943197]
16. Cook GJ, et al. Are pretreatment 18F-FDG PET tumor textural features in non-small cell lung cancer associated with response and survival after chemoradiotherapy? J Nucl Med 2013;54:19–26. [PubMed: 23204495]
17. Knogler T, et al. Three-dimensional texture analysis of contrast enhanced CT images for treatment response assessment in Hodgkin lymphoma: comparison with F-18-FDG PET. Med Phys 2014;41: 121904. [PubMed: 25471964]
18. Panth KM, et al. Is there a causal relationship between genetic changes and radiomics-based image features? An in vivo preclinical experiment with doxycycline inducible GADD34 tumor cells. Radiother Oncol 2015;116:462–6. [PubMed: 26163091]
19. Pyka T, et al. Textural features in pre-treatment [F18]-FDG-PET/CT are correlated with risk of local recurrence and disease-specific survival in early stage NSCLC patients receiving primary stereotactic radiation therapy. Radiat Oncol 2015;10:100. [PubMed: 25900186]
20. Pyka T, et al. Textural analysis of pre-therapeutic [18F]-FET-PET and its correlation with tumor grade and patient survival in high-grade gliomas. Eur J Nucl Med Mol Imaging 2016;43:133–41. [PubMed: 26219871]
21. Tixier F, et al. Intratumor heterogeneity characterized by textural features on baseline 18F-FDG PET images predicts response to concomitant radiochemotherapy in esophageal cancer. J Nucl Med 2011;52:369–78. [PubMed: 21321270]
22. Vaidya M, et al. Combined PET/CT image characteristics for radiotherapy tumor response in lung cancer. Radiother Oncol 2012;102: 239–45. [PubMed: 22098794]
23. Aghini-Lombardi F, et al. Early textural and functional alterations of left ventricular myocardium in mild hypothyroidism. Eur J Endocrinol 2006;155:3–9. [PubMed: 16793943]
24. Al-Kadi OS, Watson D. Texture analysis of aggressive and nonaggressive lung tumor CE CT images. IEEE Trans Biomed Eng 2008;55:1822–30. [PubMed: 18595800]

25. Chicklore S, et al. Quantifying tumour heterogeneity in 18F-FDG PET/CT imaging by texture analysis. Eur J Nucl Med Mol Imaging 2013;40:133–40. [PubMed: 23064544]
26. de Jong EE, et al. [18F]FDG PET/CT-based response assessment of stage IV non-small cell lung cancer treated with paclitaxel-carboplatin-bevacizumab with or without nitroglycerin patches. Eur J Nucl Med Mol Imaging 2017;44:8–16. [PubMed: 27600280]
27. Ganeshan B, et al. Hepatic enhancement in colorectal cancer: texture analysis correlates with hepatic hemodynamics and patient survival. Acad Radiol 2007;14:1520–30. [PubMed: 18035281]
28. Ganeshan B, et al. In search of biologic correlates for liver texture on portal-phase CT. Acad Radiol 2007;14:1058–68. [PubMed: 17707313]
29. Ganeshan B, et al. Tumour heterogeneity in non-small cell lung carcinoma assessed by CT texture analysis: a potential marker of survival. Eur Radiol 2012;22:796–802. [PubMed: 22086561]
30. Ganeshan B, et al. Tumour heterogeneity in oesophageal cancer assessed by CT texture analysis: preliminary evidence of an association with tumour metabolism, stage, and survival. Clin Radiol 2012;67: 157–64. [PubMed: 21943720]
31. Hatt M, et al. 18F-FDG PET uptake characterization through texture analysis: investigating the complementary nature of heterogeneity and functional tumor volume in a multi-cancer site patient cohort. J Nucl Med 2015;56:38–44. [PubMed: 25500829]
32. Engan K, et al. Exploratory data analysis of image texture and statistical features on myocardium and infarction areas in cardiac magnetic resonance images. Conf Proc IEEE Eng Med Biol Soc 2010;2010: 5728–31. [PubMed: 21097328]
33. Kotu LP, et al. Probability mapping of scarred myocardium using texture and intensity features in CMR images. Biomed Eng Online 2013;12:91. [PubMed: 24053280]
34. Awad J, et al. Texture analysis of carotid artery atherosclerosis from three-dimensional ultrasound images. Med Phys 2010;37: 1382–91. [PubMed: 20443459]
35. Coleman DP, et al. Development and validation of an in vivo analysis tool to identify changes in carotid plaque tissue types in serial 3-D ultrasound scans. Ultrasound Med Biol 2005;31:329–35. [PubMed: 15749555]
36. Madycki G, Staszkiewicz W, Gabrusiewicz A. Carotid plaque texture analysis can predict the incidence of silent brain infarcts among patients undergoing carotid endarterectomy. Eur J Vasc Endovasc Surg 2006;31:373–80. [PubMed: 16427334]
37. Niu L, et al. Surface roughness detection of arteries via texture analysis of ultrasound images for early diagnosis of atherosclerosis. PLoS One 2013;8:e76880. [PubMed: 24146940]
38. Kotze CW, et al. CT signal heterogeneity of abdominal aortic aneurysm as a possible predictive biomarker for expansion. Atherosclerosis 2014;233:510–7. [PubMed: 24530787]
39. Galavis PE, et al. Variability of textural features in FDG PET images due to different acquisition modes and reconstruction parameters. Acta Oncol 2010;49:1012–6. [PubMed: 20831489]
40. Le Pogam A, et al. Denoising of PET images by combining wavelets and curvelets for improved preservation of resolution and quantitation. Med Image Anal 2013;17:877–91. [PubMed: 23837964]
41. Teo BK, et al. Partial-volume correction in PET: validation of an iterative postreconstruction method with phantom and patient data. J Nucl Med 2007;48:802–10. [PubMed: 17475970]
42. Parmar C, et al. Robust radiomics feature quantification using semiautomatic volumetric segmentation. PLoS One 2014;9: e102107. [PubMed: 25025374]
43. Bengtsson E, Nordin B, Pedersen F. MUSE—a new tool for interactive image analysis and segmentation based on multivariate statistics. Comput Methods Programs Biomed 1994;42:181–200. [PubMed: 8062550]
44. Brunenberg E, et al. Automatic IVUS segmentation of atherosclerotic plaque with stop & go snake. Med Image Comput Comput Assist Interv 2006;9(Pt 2):9–16.
45. Kumar V, et al. Radiomics: the process and the challenges. Magn Reson Imaging 2012;30:1234–48. [PubMed: 22898692]
46. Bodenreider O, Stevens R. Bio-ontologies: current trends and future directions. Brief Bioinform 2006;7:256–74. [PubMed: 16899495]

47. National Institutes of Health. Medicine. Available at: https://www.nlm.nih.gov/healthit/snomedct/. Accessed June 12, 2017.
48. Schulz S, Marko K, Suntisrivaraporn B. Formal representation of complex SNOMED CT expressions. BMC Med Inform Decis Mak 2008;8 Suppl 1:S9. [PubMed: 19007446]
49. Schulz S, Suntisrivaraporn B, Baader F. SNOMED CT's problem list: ontologists' and logicians' therapy suggestions. Stud Health Technol Inform 2007;129(Pt 1):802–6. [PubMed: 17911827]
50. Schulz S, et al. SNOMED reaching its adolescence: ontologists' and logicians' health check. Int J Med Inform 2009;78 Suppl 1: S86–94. [PubMed: 18789754]
51. Bromuri S, et al. Multi-label classification of chronically ill patients with bag of words and supervised dimensionality reduction algorithms. J Biomed Inform 2014;51:165–75. [PubMed: 24879897]
52. Friedman C, Hripcsak G. Natural language processing and its future in medicine. Acad Med 1999;74:890–5. [PubMed: 10495728]
53. Friedman C, et al. Representing information in patient reports using natural language processing and the extensible markup language. J Am Med Inform Assoc 1999;6:76–87. [PubMed: 9925230]
54. Hripcsak G, et al. Unlocking clinical data from narrative reports: a study of natural language processing. Ann Intern Med 1995;122: 681–8. [PubMed: 7702231]
55. Nadkarni PM, Ohno-Machado L, Chapman WW. Natural language processing: an introduction. J Am Med Inform Assoc 2011;18: 544–51. [PubMed: 21846786]
56. Ohno-Machado L, Nadkarni P, Johnson K. Natural language processing: algorithms and tools to extract computable information from EHRs and from the biomedical literature. J Am Med Inform Assoc 2013;20:805. [PubMed: 23935077]
57. Powell RT, et al. Identification of histological correlates of overall survival in lower grade gliomas using a bag-of-words paradigm: a preliminary analysis based on hematoxylin & eosin stained slides from the lower grade glioma cohort of The Cancer Genome Atlas. J Pathol Inform 2017;8:9. [PubMed: 28382223]
58. Soguero-Ruiz C, et al. Support vector feature selection for early detection of anastomosis leakage from bag-of-words in electronic health records. IEEE J Biomed Health Inform 2016;20: 1404–15. [PubMed: 25312965]
59. Bird S, Klein E, Loper E. Natural language processing with python—analyzing text with the natural language toolkit. Sebastopol, CA: O'Reilly Media; 2009.
60. Garla V, et al. The Yale cTAKES extensions for document classification: architecture and application. J Am Med Inform Assoc 2011;18: 614–20. [PubMed: 21622934]
61. Savova GK, et al. Mayo clinical Text Analysis and Knowledge Extraction System (cTAKES): architecture, component evaluation and applications. J Am Med Inform Assoc 2010;17:507–13. [PubMed: 20819853]
62. Leijenaar RT, et al. Stability of FDG-PET radiomics features: an integrated analysis of test-retest and inter-observer variability. Acta Oncol 2013;52:1391–7. [PubMed: 24047337]
63. Chalkidou A, O'Doherty MJ, Marsden PK. False discovery rates in PET and CT studies with texture features: a systematic review. PLoS One 2015;10:e0124165. [PubMed: 25938522]
64. Armstrong RA. When to use the Bonferroni correction. Ophthalmic Physiol Opt 2014;34:502–8. [PubMed: 24697967]
65. Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. J R Stat Soc Series B Stat Methodol 1995;57:289–300.
66. Benjamini Y, Yekutieli D. Quantitative trait loci analysis using the false discovery rate. Genetics 2005;171:783–90. [PubMed: 15956674]
67. Ringner M, Peterson C, Khan J. Analyzing array data using supervised methods. Pharmacogenomics 2002;3:403–15. [PubMed: 12052147]
68. Storey JD. A direct approach to false discovery rates. J R Stat Soc Series B Stat Methodol 2002;64:479–98.
69. Abernethy J, Frongillo RM. A collaborative mechanism for crowdsourcing prediction problems. NIPS Proceedings 2011 Available at https://papers.nips.cc/paper/4382-a-collaborative-mechanism-for-crowdsourcing-prediction-problems.pdf. Accessed January 11, 2018.

70. Dowlin N, et al. Manual for using homomorphic encryption for bioinformatics. Proc IEEE Inst Electr Electron Eng 2017;105:552–67.

71. Dhawan AP. Collaborative paradigm of preventive, personalized, and precision medicine with point-of-care technologies. IEEE J Transl Eng Health Med 2016;4:2800908. [PubMed: 28560119]

72. Szczypinski PM, et al. MaZda—a software package for image texture analysis. Comput Methods Programs Biomed 2009;94: 66–76. [PubMed: 18922598]

73. Healthmyne. Quantitative Imaging Decision Support (QIDS). Available at: https://www.healthmyne.com/platform/. Accessed June 9, 2017.

74. ONCO Radiomics. Available at: http://www.oncoradiomics.com. Accessed June 9, 2017.

75. Valdes G, et al. MediBoost: a patient stratification tool for interpretable decision making in the era of precision medicine. Sci Rep 2016;6: 37854. [PubMed: 27901055]

76. Phillips KA, et al. "What goes around comes around": lessons learned from economic evaluations of personalized medicine applied to digital medicine. Value Health 2017;20:47–53. [PubMed: 28212968]

TAKE-HOME POINTS

- The results of radiomics-based CDS are to be subject to robust outcomes analysis, which then impacts physician behavior.
- The second phase of the translational pipeline involves the steps from clinical application to enterprise solutions, including considerations for algorithm crowdsourcing, product management, and comparative performance analytics.
- The final goal of this process is mainstream application of a clinically viable and commercially successful product that improves the standard and the value of health care.

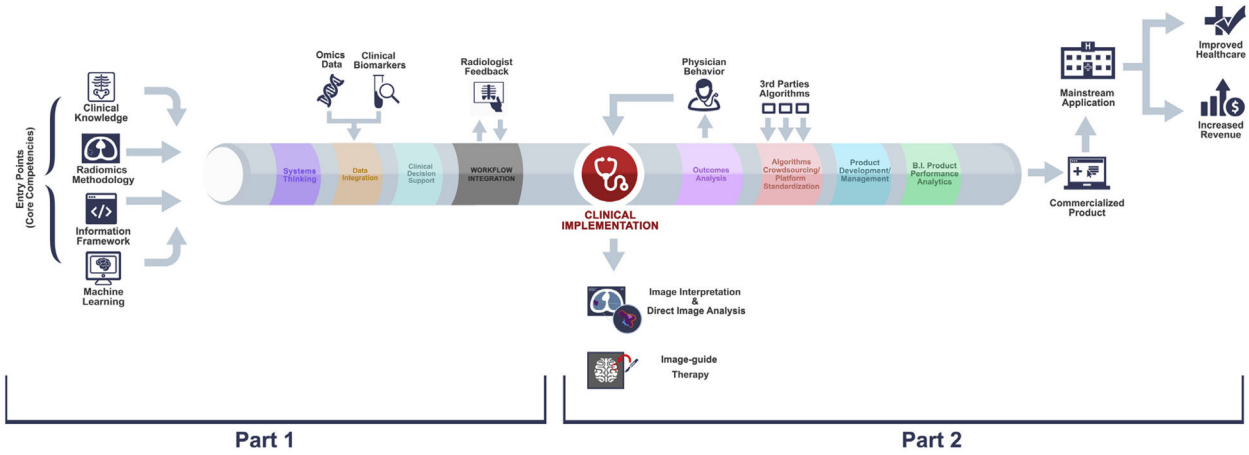

Fig 1.

The translational radiomics pipeline illustrating all the components thereof.

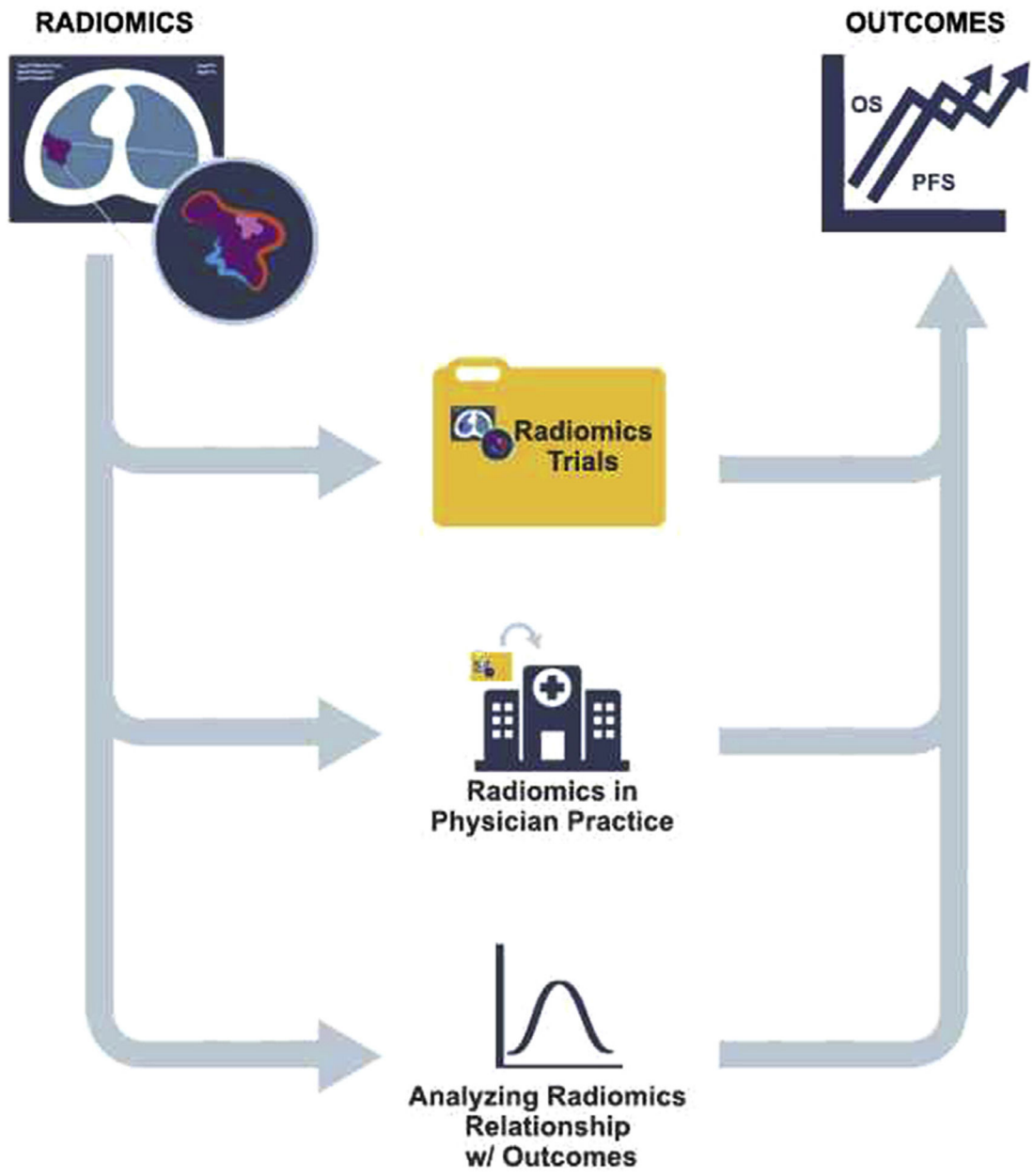

Fig 2.

Illustration of the factors involved in the outcomes analysis of radiomics. OS = outcomes survival; PFS = progression-free survival.